1.03 Urinary eicosanoids - novel biomarkers in T2-low severe asthma

Matthew Chad Eastwood[1], John Busby[1], Johan Kolmert[2], Javier Zurita[2], Sven-Erik Dahlen[2], Pamela McDowell[1], Judy Bradley[1], Craig Wheelock[2], Liam Heaney[1]
[1]Queen's University Belfast, Belfast, United Kingdom. [2]Karolinska University Hospital, Stockholm, Sweden

Abstract

Background: ~5% of patients with asthma have severe disease. Many remain symptomatic despite suppression of T2-inflammation (blood eosinophil count<0.15x109cells/L and FeNO<20ppb). What drives persistent symptoms is unclear, however, eicosanoids and obesity have been implicated in asthma pathophysiology. We hypothesized that elevated eicosanoids may contribute to persistent symptoms (Asthma Control Questionnaire-7 ≥1.5) in T2-low participants. We explored the relationship between eicosanoids, symptoms, T2-status and obesity.

Methods: Urine samples (n=91) were collected at scheduled study visits in T2-low participants during a randomized controlled trial assessing corticosteroid optimization. Samples were analysed via liquid-chromatography/mass-spectrometry. Metabolite concentrations were log2-transformed, z-scored and concentrated by pathway generating six pathway scores.

Results: Obesity was observed in “symptom-high” vs “symptom-low”, T2-low participants (Body mass index: 33.2 v 29.8 kg/m2, P=0.02). Isoprostane (0.13 v -0.14, P=0.02) and thromboxane (0.28 vs -0.08, P=0.04) pathway scores were elevated in “symptom-high” vs “symptom-low”, T2-low participants and associated with a reduced FEV1 (71.7% v 88.5%, P<0.0001). Pathway scores were not affected after adjusting for obesity (P≥0.05).

Conclusions: Thromboxane and isoprostane pathway metabolites may be acting via the thromboxane-receptor leading to increased symptoms and poorer lung function in T2-low participants. Increased metabolite production may be occurring independently of obesity in T2-low severe asthma.

Keywords: severe asthma, T2-low, urinary eicosanoids, obesity.

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